

Serial No.: 09/472,662

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Applicants note that pending claims 11, 12, and 15 were not included in either Invention I or II. Applicants have not canceled these claims as they wish to be entitled to the consideration of claims 11, 12 and 15 if a generic claim is allowed.

Attached hereto is a marked-up version of the changes made to the claims by the "Restriction and Amendment". The attached page is captioned "**Version with markings to show changes made.**"

Response to Rejection under 35 U.S.C. § 112, 2d paragraph

Claims 3-5 are rejected under 35 U.S.C. § 112, 2d paragraph, as being indefinite.

Specifically, the Examiner objects to the terms "pretreated" and "enhanced renal development and function as compared to metanephric tissue which has not been pretreated." Furthermore, the Examiner states that the term "at a suitable stage" in claim 5 renders the claim indefinite as to what stage is called suitable. Applicants respectfully traverse.

As the Examiner is aware, "[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." MPEP 2173.02.

The specification teaches that "[p]referably, the metanephric tissue is contacted with the growth factor composition *in vitro* for less than 8 hours, and preferably less than 2 hours," and "[p]referred *in vitro* temperatures are 0-10°C," see p.13, lines 16-18 of the specification.

The specification also provides ample guidance as to what "a suitable stage" means. For example, "the metanephric tissue is harvested soon after the metanephric kidney begins formation and prior to the presence of blood vessels that either originate within the metanephros or from inside or outside the metanephros," see page 11, lines 11-14 of the specification. Further, "[t]he preferred developmental stage for harvesting the metanephros will vary depending upon the species of donor... [and, g]enerally, the metanephros is harvested 1 to 5 days after the metanephros forms," see page 11, lines 21-23 of the specification.

The Examiner also pointed out an improper Markush grouping, i.e., inclusion of vitamin A as a growth factor, in claims 4-10. Applicants have corrected the relevant claims and added new claims regarding vitamin A.

Accordingly, Applicants respectfully submit that the claims in the amended form are allowable under 35 U.S.C. § 112, 2d paragraph, and request the Examiner to withdraw this rejection.

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Response to Rejection under 35 U.S.C. § 102(e)/103(a)

Claims 3-8 stand rejected under 35 U.S.C. § 102(e) or (b), as being anticipated by Zsebo *et al.* (U.S. Patent No. 6,204,363) or EP 0 853 [9]42.

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Zsebo *et al.* is directed to novel stem cell factors (SCFs), oligonucleotides encoding SCFs and methods of producing SCFs. The Examiner asserts that “[t]he reference teaches that growth enhancement of metanephric kidney tubules occur by treating said tissue with a composition comprising SCF (a growth factor, col. 3, line 63 and col. 12, lines 34-39 and lines 66+).” Applicants respectfully traverse.

Zsebo *et al.* mentions “metanephric kidney tubules” at col. 13, lines 39-40 wherein Zsebo states “Enhancement of growth in non-hematopoietic stem cells such as ... mesonephric and metanephric kidney tubules... is of benefit in states where specific tissue damage has occurred to these sites.” Although it teaches SCF may be useful in treating neurological damages, intestinal damages or infertility, the reference does not teach or suggest treatment of embryonic metanephric tissue with SCF. Where transplantation is described, the reference teaches that “SCF is useful for expanding early hematopoietic progenitors in syngeneic, allogenic, or autologous bone marrow transplantation,” and therefore bone marrow can be “treated in vitro to activate or expand the cell number prior to transplantation.” See Zsebo *et al.* at col. 14, lines 18-19. The reference is completely silent with respect to treatment of metanephric tissue prior to transplantation with a growth factor.

Therefore, Applicants respectfully submit that Zsebo *et al.* does not anticipate the claims of the invention.

EP 0 853 942 teaches the use of embryonic metanephric tissue from a donor in a method of increasing the functioning nephron mass of a recipient by implanting the metanephric tissue next to the recipient’s omentum or under the renal capsule of the recipient’s kidney. EP 0 853 942 further discloses growth factor (including VEGF) treatment of metanephric tissue at the time of and/or after transplantation, but is silent with respect to growth factor treatment of metanephric tissue before transplantation.

Applicants further submit that EP 0 853 942 cannot be construed as to “inherently” describe the element of growth factor treatment of metanephric tissue before transplantation, because EP 0 853 942 teaches away from contacting metanephric tissue for transplantation *in vitro* prior to the transplanting operation. On p. 4, line 31-32, the reference explicitly points out, “[metanephroi] should be transplanted as

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soon as possible into the recipient, preferably within one hour after removal from the embryonic donor, and more preferably within 30 minutes."

Therefore, Applicants respectfully submit that EP 0 853 942 does not anticipate the claims of the present invention.

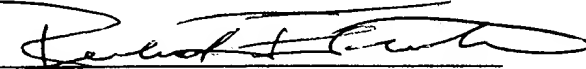
Accordingly, Applicants request the Examiner to withdraw this rejection.

Applicants submit that the claims are now in condition for allowance and an early notification of such is solicited. Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) Embryonic metanephric tissue which has been pretreated with a growth factor composition comprising at least one growth factor for metanephric development wherein said pretreated metanephric tissue has enhanced renal development or function upon transplantation into recipients as compared to similarly transplanted metanephric tissue which has not been pretreated with said growth factor composition.

4. (Amended) The embryonic metanephric tissue of claim 3 [4] wherein said growth factor is selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, [vitamin A,] and growth hormone.

5. A method for the treatment of embryonic metanephric tissue comprising contacting embryonic metanephric tissue obtained from a donor at a suitable stage of embryonic development with a growth factor composition comprising a growth factor for metanephric development.

6. (Amended) The method of claim 5 wherein said growth factor is selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, [vitamin A,] and growth hormone.

7. The method of claim 5 wherein said treatment is *in vivo*.

8. The method of claim 7 wherein said treatment occurs during ureteroureterostomy.

9. The method of claim 5 wherein said treatment is *ex vivo*.

10. The method of claim 9 further comprising the step of transplanting said embryonic metanephric tissue into a recipient.

11. (Amended) A growth factor composition for en[c]hancing the growth and development of embryonic metanephric tissue comprising two or more growth factors for metanephric development.

12. (Amended) The growth factor composition of claim 11 wherein said two or more growth factors are selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, [vitamin A,] and growth hormone.

New claims:

13. (New) The embryonic metanephric tissue of claim 3 wherein said growth factor composition comprises vitamin A.

14. (New) The method of claim 5 wherein said growth factor composition comprises vitamin A.

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15. (New) The growth factor composition of claim 11 wherein said growth factor composition comprises vitamin A.

APPENDIX OF PENDING CLAIMS

3. Embryonic metanephric tissue which has been pretreated with a growth factor composition comprising at least one growth factor for metanephric development wherein said pretreated metanephric tissue has enhanced renal development or function upon transplantation into recipients as compared to similarly transplanted metanephric tissue which has not been pretreated with said growth factor composition.
4. The embryonic metanephric tissue of claim 3 wherein said growth factor is selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, and growth hormone.
5. A method for the treatment of embryonic metanephric tissue comprising contacting embryonic metanephric tissue obtained from a donor at a suitable stage of embryonic development with a growth factor composition comprising a growth factor for metanephric development.
6. The method of claim 5 wherein said growth factor is selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, and growth hormone.
7. The method of claim 5 wherein said treatment is *in vivo*.
8. The method of claim 7 wherein said treatment occurs during ureteroureterostomy.
9. The method of claim 5 wherein said treatment is *ex vivo*.
10. The method of claim 9 further comprising the step of transplanting said embryonic metanephric tissue into a recipient.
11. A growth factor composition for enhancing the growth and development of embryonic metanephric tissue comprising two or more growth factors for metanephric development.
12. The growth factor composition of claim 11 wherein said two or more growth factors are selected from the group consisting of insulin-like growth factor I, insulin-like growth factor II, vascular endothelial growth factor, transforming growth factor alpha, transforming growth factor beta, hepatocyte growth factor, fibroblast growth factors, platelet-derived growth factor, leukemia inhibitory factor, angiopoetins 1 and 2, bone morphogenetic proteins, nerve growth factor, and growth hormone.

New claims:

13. The embryonic metanephric tissue of claim 3 wherein said growth factor composition comprises vitamin A.

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14. The method of claim 5 wherein said growth factor composition comprises vitamin A.
15. The growth factor composition of claim 11 wherein said growth factor composition comprises vitamin A.